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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,939	02/19/2002	Leon W.M.M. Terstappen	Immu.Rapid	6526
40541	7590	08/26/2005	EXAMINER	
IMMUNICON CORPORATION 3401 MASONS MILL ROAD SUITE 100 HUNTINGDON VALLEY, PA 19006			YU, MISOOK	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/079,939

Applicant(s)

TERSTAPPEN ET AL.

Examiner

MISOOK YU, Ph.D

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19,24-28,84 and 85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19,24-28,84 and 85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 10/17/03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Exhibit A.

DETAILED ACTION***Election/Restrictions***

Applicant's election of group I in the reply filed on 06/02/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-19, 24-28, 84, and 85 are pending and examined on merits as they are drawn to HER-2 as the elected species for the first genus and cell spotter analysis as the second genus.

Claim Objections

Claims 1-19, 24-28, 84, and 85 are objected to because of the following informalities. Claims as currently construed use two different terms "tumor diathesis-associated molecule", and "tumor diathesis associated molecule" for a single entity. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19, 24-28, 84, and 85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing because the preamble of claims 1-19, 24-28, 84, and 85 says that the claimed invention is for assessing a patient for the presence of a malignancy, and step d) of the base claim 1 says that detection of labeled

Art Unit: 1642

cells indicate a person has a malignancy. In addition, the step d) in the base claim goes on saying that the claimed invention is looking for alteration in at least one tumor diathesis-associated molecule. However, the claims do not say how the additional step of looking for alteration in at least one tumor diathesis-associated molecule is associated with the preamble of the claim. Preamble does not say anything about severity while the conclusion step does.

Claims 5, 16, and 85 contain the trademark/trade name "Cell Spotter". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe "Cell Spotter" and, accordingly, the identification/description is indefinite.

Claim 6 is confusing because it is not clear how claim 6 is related to the purpose set out in the preamble of the claimed method.

Claim 8 is confusing because it is not clear how claim 8 is related to the purpose set out in the preamble of the claimed method, and also confusing as to how the sensitivity of the malignant cell is determined.

Art Unit: 1642

Claim 13 recites the limitation "said ligand" in line 1. There is insufficient antecedent basis for this limitation in the claim. For the compact prosecution purpose, the unclear antecedent lacking limitation would be interpreted as EpCAM antibody based on the claim amendment history in this Office action. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claims 17-19, 24, 26, 27, and 28 are confusing as to how all of these methods are related to the purpose of the claimed invention set out in the preamble of the claims. The elected invention to be examined is drawn to method of detecting a malignancy

Claim 25 depends on the cancelled claim 22, and the Office could not determine how the step in claim 25 is related to the claimed invention of method of assessing whether a patient has a malignancy.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19, 24-28, 84, and 85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for carcinoma detection, does not reasonably provide enablement for any other malignancy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This rejection has two parts.

Art Unit: 1642

The claimed invention is drawn to method of assessing whether one has a malignancy using the claimed active steps.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is Aundue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification is about inventors' discovery of ways of early detection of carcinoma shedding by way of enriching circulating epithelial cells. However, the specification does not teach how to use the claimed invention to assess whether one has hematopoietic cancers. Rubin et al., Blood. 1990 Dec 15;76(12):2594-8 teach malignancy includes hematopoietic cancers, such as acute myeloid leukemia.

Racila et al., inventors' own peer reviewed journal publication, IDS C16, Proc Natl Acad Sci U S A. 1998 Apr 14;95(8):4589-94, teach that carcinoma (epithelial cancer) cells are shed in into a system containing hematopoietic cells (i.e. circulatory system) resulting in presence of epithelial cells in small quantity in mostly hematopoietic background. Detecting circulating epithelial cancer cells are possible through enriching the circulating epithelial cells using the antibody binding to epithelial adhesion molecule, followed by detecting cancer cells using

Art Unit: 1642

a cancer marker (cytokeratin positive) in the epithelial cell. In summary, Racila teach that only epithelial cancer in hematopoietic background could be enriched using EpCAM antibody. EpCAM antibody in base claim 1 would not be able to enrich any other cancer cells in hematopoietic background. Limiting the scope to carcinoma would obviate this part of rejection.

In addition, claims 2-4 while being enabling for labeling non-hematopoietic cells, are not enabled for labeling both the hematopoietic cells, and non-hematopoietic cells. Claims 2-4 are drawn to method of cancer cell detection by labeling both hematopoietic cells, and non-hematopoietic cells, followed by detecting presence and number of labeled cells, in order to determine whether one has a malignancy. The specification does not guide one of skill to analyze the sample with labeled malignant cells, labeled hematopoietic cells, and labeled tumor diathesis associated molecule for the purpose stated in the preamble of the claims.

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad scope of the claims, it is concluded that undue experimentation is required to practice the invention.

Claims 1-19, 24-28, 84, and 85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in

Art Unit: 1642

such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This **new matter** rejection is made because claims 1, and 12 as currently construed define EpCAM antibody used in claims 1-19, 24-28, 84, and 85 as an antibody "specific for at least one cancer cell determinant". However, the specification as originally filed at page 59 lines 1-10 discloses that monoclonal antibodies specific for epithelial cell adhesion molecule (EpCAM) are broadly reactive with tissue of epithelial cell origin. In other words, EpCAM antibody is not specific for at least one cancer cell determinant, but specific for epithelial cells not cancer cells. Note inventors' own peer-reviewed journal publication, i.e. Racila et al., IDS C16, Proc Natl Acad Sci U S A. 1998 Apr 14;95(8):4589-94 regarding EPCAM antibody of GA73.3. Although some claims do not specifically recite EpCAM antibody, all of the pending claims require EpCAM antibody. Therefore all claims are included in this rejection.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) to 60/074,535 is acknowledged. The provisional application data sheet originally filed lists Dr. Jonathan W. Uhr as the inventive entity while the later filed communication appears to indicate that Jonathan W. Uhr, David Scheinberg and Ronald Finn are the inventive entity. Note the attached Exhibit A.

In response to the petition to correct the inventorship filed on 02/09/1999, the Office sent a letter on 03/04/99 (a copy included as page 3 of the attached Exhibit A) to the applicant, stating that the Office could not comply with the

Art Unit: 1642

request because of the error on applicant's part, i.e. the required address of Dr. Leon W. M. Terstappen had not been supplied to the Office. The Office does not have any record that applicant has responded to the letter the Office mailed on 03/04/99. Since the petition to correct inventorship had not been complete, Dr. Leon W. M. Terstappen does not belong to the inventive entity of the provisional application 60/074,535. Based on the facts above, the priority claim under 35 U.S.C. 119(e) to 60/074,535 is denied.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6, 7, 15, and 84 are rejected under 35 U.S.C. 102(b) as being anticipated by Cote et al., J Clin Oncol. 1991 Oct;9(10):1749-56.

Claims 1, 5, 6, 7, 15, 16, and 84 are drawn to method comprising obtaining biological specimen (after cancer treatment in claim 6, and periodically in claim 7) containing hematopoietic and non-hematopoietic malignant cells, preparing a sample by adding detectably labeled EpCAM (epithelial adhesion molecule) antibody to the specimen, contacting the sample with one reagent which specifically labels malignant cells, followed by determining the presence and number of labeled cancer cells using the various assay method in claim 5, wherein the detection of the labeled cells indicating the patient has a malignancy,

Art Unit: 1642

the greater the number of cells present, the greater the severity of the malignancy, and the claimed method further comprises assessment of the labeled cells for alterations of Her-2 in claims 6, 15, and 84 (as the elected tumor associated diathesis molecule), and Her-2 is assessed with the various art-known method in claim 16.

The specification discloses at paragraph [0111] "The EpCAM antigen is expressed on cells of epithelial origin, but not on cells of hematopoietic origin", and at paragraph [0210] "monoclonal antibodies (Mabs) specific for epithelial cell adhesion molecule (EpCAM) are broadly reactive with tissue of epithelial cell origin". Based on this description of EpCAM antigen, the Office interprets that any antibody specific for cells of epithelial origin, but not on cells of hematopoietic origin, and broadly reactive with tissue of epithelial cell origin, belongs to the genus of the antibodies recited as "EpCAM antibody" (note the base claim 1) being used in the instantly claimed method.

Cote et al., teach method of obtaining biological specimen containing hematopoietic and non-hematopoietic malignant cells, i.e. bone marrow aspirates (note page 1753, bone marrow aspirates of breast cancer patients contains and non-hematopoietic malignant cells) from breast cancer patients who underwent surgery (note Fig. 1 for the periodic assessment), preparing a sample by adding detectably labeled monoclonal antibodies that meets the scope of "EpCAM antibody" (epithelial specific antibody, but not on cells of hematopoietic origin on page 1750, left column under the subheading *Monoclonal Antibodies*) to the specimen, contacting the sample with one reagent (anti-keratin antibody, also

Art Unit: 1642

note page 1750, left column) which specifically labels malignant cells, followed by determining the presence and number of labeled cancer cells using the immunofluorescent assay method. Cote et al., concludes bone marrow tumor burden (number of cancer cells being present) is correlated with bad outcome for the patients, i.e. recurrence of breast tumor, thus anticipating the conclusion of the instantly claimed invention. In addition, Cote et al., teach alterations of Her-2 in tumor patients at page 1754-1755.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5, 9, 10, 11, 12, 13, 14, 16, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naume et al., J Hematother. 1997 Apr;6(2):103-14 in view of Cote et al., (cited above).

The preamble of the base claim 1 says that the claimed invention is drawn to method of assessing whether one has a malignancy. The active steps after the transitional phrase "comprising" say that the purpose of the claimed method set out in the preamble of the claimed invention is accomplished by steps a)-d), wherein step a) specify that a biological specimen containing hematopoietic and non-hematopoietic malignant cells are obtained, followed by preparing a sample (one of the sample being immunomagnetic sample comprising the biological

Art Unit: 1642

specimen mixed with magnetic particles coupled to EpCAM antibody in claim 9) by mixing the biological specimen obtained in step a) with a detectably labeled EpCAM antibody in step b), followed by contacting the sample in step b) with one reagent which specifically labels malignant cells in step c), followed by determining the presence and number of labeled cancer cells using the various assay method in claim 5, wherein the detection of the labeled cells indicates the patient has a malignancy. The conclusion step of claim 1 also says that the greater the number of cells present, the greater the severity of the malignancy and the claimed method further comprises assessment of the labeled cells for alterations in at least on tumor diathesis-associated molecule.

The specification at Example 3 on bottom half of page 58 discloses that blood from patient having breast carcinoma is a biological specimen containing hematopoietic and non-hematopoietic malignant cells and also discloses on page 59 lines 1-10 discloses that monoclonal antibodies specific for epithelial cell adhesion molecule (EpCAM) are broadly reactive with tissue of epithelial cell origin.

Naume et al., teach blood samples (note page 105, left column, the heading *Collection of BM and PB*) and BerEP4 mAb, 317G5 mAb, MOC31 mAb reacting with epithelial cells (note the heading *Monoclonal antibodies* at page 104) being mixed, followed by immunomagnetic separation and then labeling the separated epithelial cells with AE3 anticytokeratin mAb, AE1 anticytokeratin mAb, A45-B/B3 mAb (reacts with various keratin) and counting the labeled cells (data shown at Table 4 on page 110).

Art Unit: 1642

Naume et al., do not teach the step assessing alteration in Her-2 (the elected species of tumor diathesis associated molecule).

However, Cote et al., teach that alternation of Her-2 in a malignancy had been well known before the effective filing date of the instant application.

Therefore it would have been obvious to one of skill in the ordinary skill to make and use the claimed invention with a reasonable expectation of success, Naume et al., teach how to enrich circulating epithelial cells, and how to detect and enumerate the enriched circulating cancer cells, and given teaching of Cote et al., that alternation in Her-2 is associated with a malignancy. One of ordinary skill would be motivated to assess Her-2 given teachings of Cote et al., at page 1755 "By using the bone marrow status in conjunction with established prognostic parametes and other promising markers such as ...Her-2/neu gene amplication,...it may be possible to identify patients who are at increased rish for tumor progression". In other words, Cote et al., teach the multiple parameters are more reliable diagnostic tools than a single parameter.

Claims 1, 8, 17-19, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naume et al (cite above) in view of Cote et al (cited above) and further in view of Rubinstein et al., J Natl Cancer Inst. 1990 Jul 4;82(13):1113-8

Claims 1, 8, 17-19, and 24 are drawn to method of assessing whether one has a malignancy by the method described in the base claim 1 (note the art rejections for further details about the base claim), the claimed method further

Art Unit: 1642

comprising contacting the malignant cells of the base claim with chemotherapeutic agent to assess sensitivity (claim 8), isolating and culturing malignant cells, expanding malignant cells, followed by contacting the cells with chemotherapeutic agent to assess sensitivity (claims 17, 18, and 24), and assessing Her-2 status in the cultured cells (claim 19).

Naume et al., teach all the limitations in base claim 1 (Note the 103 rejection above.) except the steps of contacting the cells with chemotherapeutic agent, expanding the cells, and assessing Her-2.

Cote et al., teach Her-2 alternation is a good parameter for assessing a malignancy.

Neither Naume et al., nor Cote et al., teach isolating and culturing malignant cells, expanding malignant cells, and contacting the cells with chemotherapeutic agent to assess sensitivity the malignant cells with chemotherapeutic agent to assess sensitivity. However, Rubinstein et al., teach that isolating and expanding tumor cells, and anti-tumor agent screening had been well known before the effective filing date of the instant application.

Therefore it would have been obvious to one of skill in the ordinary skill to make and use the claimed invention with a reasonable expectation of success to select potential anti-tumor agents, given teaching of Rubinstein et al., that the anti-tumor agent screening art already had the knowledge how to isolate, and generate cancer cells from various malignancy. One of ordinary skill would be motivated to screen a potentially effective anti-cancer drug using a cell line cells instead of using an in vivo subject because it is cost-effective.

Art Unit: 1642

Claims 1 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cote et al (cited above) in view of Bonaldo et al., Genome Res, 09/1996, vol. 6, pages 791-806.

Note interpretation of claim 1 above. Claims 26-28 not rejected above are interpreted as drawn to assessing Her-2 (the elected species) with the various assay method recited in claims 26-28.

Note what Cote et al., teach above. Cote et al., do not teach the specifically recited assay in the instant claims 26-28. However, Bonaldo et al., teach that the recited assay had been well known in the art before the effective filing date of the instant application.

Therefore it would have been obvious to one of skill in the ordinary skill to make and use the claimed invention with a reasonable expectation of success, given teaching of Cote et al., that alteration of Her-2 in a malignancy, and Bonaldo et al., teach that the instantly recited assay had been well known in the art before the effective filing date of the instant application. One of ordinary skill would be motivated to use the claimed nucleic acid detection method given Bonaldo et al., teach those nucleic acids assays are reliable.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

Art Unit: 1642

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-15, 26, and 84 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,365,362.

Although the conflicting claims are not identical, they are not patentably distinct from each other. One way obviousness applies to double patenting rejection. The instantly claimed invention and the patented claims are not identical in that the instantly claimed invention uses "EpCAM antibody" while the claims in the patent uses genus of ligands, which EpCAM antibody" is a sub-genus recited in claim 9 of the patent.

The instant application at Example 3 on bottom half of page 58 discloses that blood from patient having breast carcinoma is a biological specimen containing hematopoietic and non-hematopoietic malignant cells. The blood of a test subject suspected of having early stage cancer in claim 1 of the patent is a species of the recited specimen in the instant claim 1.

The claims of the patent do not say the method further comprises assessing Her-2 (the elected species of tumor diathesis-associated molecule) as recited in the instant claims. However, Cote et al., teach that alterations of Her-2 in a malignancy has been known before the effective filing date of the instant application.

Art Unit: 1642

The instant claims 9, and 11 together makes up the colloidal immunomagnetic particle used in the claim 1 of U.S. Patent No. 6,365,362.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

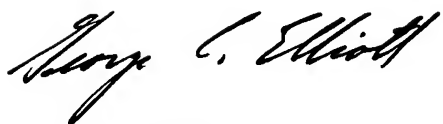
MISOOK YU, Ph.D
Examiner

Art Unit: 1642

Art Unit 1642



**MISOOK YU
PATENT EXAMINER**



**DIRECTOR
TECHNOLOGY CENTER 1600**



Exhibit A

Page 1 of 3

A/prov

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INTELLECTUAL PROPERTY LAW
(PATENT, BIOTECHNOLOGY, COMPUTER,
TRADEMARK & TRADE SECRET LAW)

February 12, 1998

PROVISIONAL APPLICATION COVER SHEET

Transmitted herewith for filing in the U.S. Patent Office is the attached provisional patent application (Docket No. 6079) entitled: *Test for Detecting, Enumerating and Characterizing Carcinoma Cells in the Blood.*

Inventors

Full Name of Inventor: Jonathan W. Uhr

Residence Address: 12311 Shiremont, Dallas, Texas 75230

Correspondence

Please direct any correspondence to Benjamin Aaron Adler, Ph.D., J.D. at the address shown above.

Respectfully submitted,

Benjamin Aaron Adler, Ph.D., J.D.
Counsel for Applicant
Registration No. 35,423

Date: 2/12/98

50074335-021298

Exhibit A

page 2 of 3



UNITED STATES PATENT AND TRADEMARK OFFICE

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Bib Data Sheet

CONFIRMATION NO. 4290

SERIAL NUMBER 60/074,535	FILING DATE 02/12/1998 RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
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APPLICANTS

JONATHAN W. UHR, DALLAS, TX;

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 RONALD D. FINN, RYE, NY; MICHAEL R. DEWITT, BRONX, NY;

** CONTINUING DATA *****

** FOREIGN APPLICATIONS *****

IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** SMALL ENTITY **
 ** 05/13/1998

Foreign Priority claimed 35 USC 119 (a-d) conditions met	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> Met after Allowance	STATE OR COUNTRY TX	SHEETS DRAWING 4	TOTAL CLAIMS	INDEPENDENT CLAIMS
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Verified and Acknowledged

Examiner's Signature _____ Initials _____

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 HOUSTON, TX
 772710509

TITLE

TEST FOR DETECTING, ENUMERATING AND CHARACTERIZING CARCINOMA CELLS IN THE BLOOD

FILING FEE RECEIVED 100	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	<input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue)
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OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Page 3 of 3

Exhibit A

Date: 3/4/99

Application Number: 60/074535

Dear Applicant or Attorney of Record:

response to your request for:

- () A duplicate filing receipt. Our records indicate that an official filing receipt was mailed on _____.
- () A corrected filing receipt, due to applicant's error. We are unable to comply with your request due to your failure to submit the proper fee for this service. The following information is cited for your convenience:

37 CFR 1.19

Patent and Trademark Office will supply copies of the following documents upon payment of the fees indicated:

(h) Additional filing receipts

Duplicate.....\$25.00

Corrected due to applicant error....\$25.00

- () Enclosed is the official filing receipt that was mailed to the address given at time of filing; the filing receipt was returned marked "return to sender, address unknown, etc." A review of the Declaration gives this address as your mailing address. A change of address should be forwarded to the Group Art Unit handling your application to prevent future errors of this type.

(X) Other: A corrected filing receipt, due to applicant error. We are unable to comply with your request due to your failure to submit the residence of Leon W.M.M. Teistappen

OIE - Unit 5
ps Correction Examiner
Publication Processing Division
3) 308 - 8997